Fairfax Cryobank
The Trusted Choice for Donor Sperm

Donor 4390

Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 03/11/24

Donor Reported Ancestry: Irish, German Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by genotyping of 99 mutations in the CFTR gene	1/300
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/610
Hb Beta Chain-Related Hemoglobinopathy (including Beta Thalassemia and Sickle Cell Disease) by genotyping	Negative for 28 mutations tested in the HBB gene	1/290
Tay Sachs Enzyme Testing	Non carrier by Hexosaminidase A activity	
Special Testing		
Homocystinuria CBS Related	Negative by gene sequencing in the CBS gene	1/627
Very Long Chain Acyl CoA Dehydrogenase Deficiency (ACADVL)	Negative by gene sequencing in the ACADVL gene	1/261
VPS53 Related Disorders	Negative by gene sequencing in the VPS53 gene	
Based on the report of a child with Autosomal Recessive Ectodermal Dysplasia. Confirmed by donor testing March 2024 – see attached.	Carrier: Autosomal Recessive Ectodermal Dysplasia (WTN10A) Donor variant: c. 910A>C(p.Asn304His)	Partner testing is recommended for WTN10A before using this donor.
Gene: PEX6	Negative by gene sequencing	

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.**Donor residual risk is the chance the donor is still a carrier after testing negative.

Counsyl

RESULTS RECIPIENT
FAIRFA .YOBANK [redacted]
[redacted]
Report Date: 07/16/2014

MALE
DONOR 4390
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 07/09/2014
Date Received: 07/11/2014
Date Tested: 07/16/2014
Barcode: [redacted]
Indication: Egg or Sperm Donor

FEMALE
N/A

Family Prep Screen

NEGATIVE

ABOUT THIS TEST

The Counsyl Family Prep Screen (version 1.0) tests known mutations to help you learn about your chance to have a child with a genetic disease.

PANEL DETAILS

Fairfax Cryobank Fundamental Panel **(3 diseases tested)**

VERSION

DONOR 4390 **(Family Prep Screen 1.0)**

RESULTS SUMMARY

NEGATIVE
No known or potential disease-causing mutations were detected.

ENTERED
DH 8-1-14

CLINICAL NOTES

- None

NEXT STEPS

- If necessary, patients can discuss residual risks with their physician or a genetic counselor.
- To schedule a complimentary appointment to speak with a clinical expert about these results, please visit counsyl.com/my/consults/.

Methods and Limitations

DONOR 4390 [Family Prep Screen 1.0]: targeted genotyping and copy number analysis.

Targeted genotyping: Targeted DNA mutation analysis is used to simultaneously determine the genotype of 127 variants associated with 2 diseases. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

Copy number analysis: Targeted copy number analysis is used to determine the copy number of exon 7 of the SMN1 gene relative to other genes. Other mutations may interfere with this analysis. Some individuals with two copies of SMN1 are carriers with two SMN1 genes on one chromosome and a SMN1 deletion on the other chromosome. In addition, a small percentage of SMA cases are caused by nondeletion mutations in the SMN1 gene. Thus, a test result of two SMN1 copies significantly reduces the risk of being a carrier; however, there is still a residual risk of being a carrier and subsequently a small risk of future affected offspring for individuals with two or more SMN1 gene copies. Some SMA cases arise as the result of de novo mutation events which will not be detected by carrier testing.

Limitations: In an unknown number of cases, nearby genetic variants may interfere with mutation detection. Other possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. If more than one variant is detected in a gene, additional studies may be necessary to determine if those variants lie on the same chromosome or different chromosomes. The Counsyl test does not fully address all inherited forms of intellectual disability, birth defects and genetic disease. A family history of any of these conditions may warrant additional evaluation. Furthermore, not all mutations will be identified in the genes analyzed and additional testing may be beneficial for some patients. For example, individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathies, which can be identified by CBC and hemoglobin electrophoresis or HPLC (*ACOG Practice Bulletin No. 78. Obstet. Gynecol. 2007;109:229-37*).

This test was developed and its performance characteristics determined by Counsyl, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's workup. CLIA Number: **#05D1102604.**

LAB DIRECTORS

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Jelena Brezo

Jelena Brezo, PhD, FACMG

Diseases Tested

Autosomal Recessive Disorders

TARGETED GENOTYPING

Cystic Fibrosis - Gene: CFTR. **Variants (99):** G85E, R117H, R334W, R347P, A455E, G542*, G551D, R553*, R560T, R1162*, W1282*, N1303K, c.1521_1523delCTT, c.1519_1521delATC, c.2052delA, c.3528delC, c.489+1G>T, c.579+1G>T, c.1585-1G>A, c.1766+1G>A, 2789+5G>A, c.2988+1G>A, 3849+10kbC>T, E60*, R75*, E92*, Y122*, G178R, R347H, Q493*, V520F, S549N, P574H, M1101K, D1152H, c.2012delT, c.262_263delTT, c.313delA, c.948delT, c.3744delA, c.3773dupT, c.1680-1G>A, 3272-26A>G, c.2051_2052delAAinsG, S549R, R117C, L206W, G330*, T338I, R352Q, S364P, G480C, C524*, S549R, Q552*, A559T, G622D, R709*, K710*, R764*, Q890*, R1066C, W1089*, Y1092X, R1158*, S1196*, W1204*, Q1238*, S1251N, S1255*, c.3067_3072del6, c.442delA, c.531delT, c.803delA, c.805_806delAT, c.1545_1546delTA, M607_Q643del, c.1911delG, c.1923_1931del9ins1, c.1976delA, c.3039delC, c.3536_3539delCCAA, c.3659delC, c.1155_1156dupTA, c.2052dupA, c.2175dupA, c.2738insG, 296+12T>C, c.273+1G>A, 405+3A>C, c.274-1G>A, 711+5G>A, c.580-1G>T, c.1766+1G>T, 1898+5G>T, Q996, c.325_327delTATinsG, 3849+4A>G, c.1075_1079del5ins5. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection rate:** Northern European 91%.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - Gene: HBB. **Variants (28):** E7V, K18*, Q40*, c.126_129delCTTT, c.27dupG, IVS-II-654, IVS-II-745, c.315+1G>A, IVS-I-6, IVS-I-110, IVS-I-5, c.92+1G>A, -88C>T, -28A>G, -29A>G, c.25_26delAA, c.217dupA, c.316-2A>C, c.316-2A>G, G25, -87C>G, E7K, W16*, c.51delC, c.20delA, E27K, E122Q, E122K. **Detection rate:** Northern European 83%.

COPY NUMBER ANALYSIS

Spinal Muscular Atrophy - Gene: SMN1. **Variant (1):** SMN1 copy number. **Detection rate:** Northern European 95%.

Risk Calculations

Below are the risk calculations for all diseases tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents the patient's post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patient's future children could inherit each disease. These risks are inherent to all carrier screening tests, may vary by ethnicity, are predicated on a negative family history and are present even after a negative test result. Inaccurate reporting of ethnicity may cause errors in risk calculation.

Disease	DONOR 4390 Residual Risk	Reproductive Risk
Cystic Fibrosis	1 in 300	1 in 33,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	1 in 290	1 in 58,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000

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[redacted]

Patient Information
4390, Donor
DOB: [redacted]
Sex: M
MR#: 4390
FD Patient#: [redacted]

Accession:
[redacted]
FD Test#: [redacted]
Order#: [redacted]
Ext Test#: [redacted]
Ext Order#: [redacted]
Specimen Type: DNA
Collected: Not Provided
Received Date: Oct 31, 2023
Authorized Date: Feb 20, 2024

Physician:
Seitz, Suzanne
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031 US

Laboratory:
Fulgent Genetics
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Mar 9, 2024**

FINAL Report

TEST PERFORMED

Known Mutation / Site-Specific Testing
(1 Variant)

RESULTS:

1 VARIANT DETECTED

Gene Info		Variant Info			
GENE	INHERITANCE	VARIANT	ZYGOSITY	CLASSIFICATION	RESULTS
WNT10A NM_025216.3	Autosomal Dominant & Autosomal Recessive	c.910A>C p.Asn304His	Heterozygous	**Likely Pathogenic**	**DETECTED**

INTERPRETATION:

Notes and Recommendations:

- Genetic counseling is recommended.
- These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.

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The targeted test results for the specimen reported here indicate that NM_025216.3:c.910A>C (p.Asn304His) in the WNT10A gene was **detected** (heterozygous) in this individual. Biallelic mutations of WNT10A are associated with odontoonychodermal dysplasia (OODD) and Schopf-Schulz-Passarge syndrome, while autosomal recessive or autosomal dominant mutations in WNT10A are associated with selective tooth agenesis-4 (STHAG4) (PubMed: 29772684; OMIM: 606268). Autosomal dominant phenotypes have also been described to include dry skin, abnormal sweating, nail abnormalities and sparse hair in some patients (OMIM: 150400). This variant has been reported in the compound heterozygous state in three unrelated individuals with WNT10A-related conditions (Invitae; personal communcation). This variant has not been reported in the Broad dataset (individuals without severe childhood onset disease). The physiochemical difference between Asn and His as measured by Grantham's Distance is 68. This score is considered a moderate change (PubMed: 4843792, 6442359). Analysis of amino acid conservation indicates that the wild-type amino acid, Asn304, is conserved in all 53 mammals examined including 11 primates, and in 35/37 non-mammalian vertebrates, increasing the likelihood that a change at this position would not be tolerated. Predictive algorithms: 8/10 deleterious (FATHMMMKL, LRT, METALR, METASVM, MUTATIONASSESSOR, MUTATIONTASTER, PROVEAN, SIFT); 2/10 tolerated (AGVGD, FATHMM)). The laboratory considers this variant to be likely pathogenic.

GENES TESTED:

Known Mutation Test

1 gene tested.

WNT10A

METHODS:

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). Methodology - Next Generation Sequencing (NGS), Sanger Sequencing, quantitative PCR (qPCR), repeat-primed PCR (rpPCR) or multiplex ligation-dependent probe amplification (MLPA) is selected by the laboratory to provide optimal results.

If NGS was performed:
DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37 / hg19), variants were detected in regions of at least 10x coverage. The known mutation genomic loci requested are evaluated for the presence or absence of variation compared to the human genome reference sequence. Bioinformatics: Fulgent Germline Pipeline v2019.1 or v2019.2 was used to generate variant calls for this test.

If Sanger Sequencing was performed:
DNA was amplified for the target region and sequenced bi-directionally using an ABI 3730XL instrument. The data was analyzed against the reference gene sequence and the known variant position as requested.

If qPCR was performed:
DNA was amplified for the target region and quantified using a QuantStudio 6 instrument. The data is compared to control genes and control individuals for the targets as requested.

If rpPCR was performed:
This analysis is performed by repeat-primed PCR (rpPCR) and amplicon length analysis. The scope of this assay is limited to repeat expansion analysis of the specified gene. Gene sequencing and deletion/duplication analysis are not included in this assay. This analysis does not include methylation studies.

If MLPA was performed:
DNA was amplified for the target regions and quantified using probesets using kits from MRC-Holland and an ABI 3730 instrument.The data is compared to control genes and control individuals for the targets as requested.

LIMITATIONS:

All laboratory tests have limitations. These results assume that the specimen received in the laboratory belongs to the named individual and that no mix-up or co-mingling of specimens has occurred. Positive results do not imply that there are no other pathogenic alterations in the patient's genome, and negative results do not rule out a genetic cause for the indication for testing. This assay assumes that any stated familial relationships are accurate. This assay is not designed or validated for the detection of

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somatic mosaicism or somatic mutations. This assay will only analyze the variant(s) requested. It is possible that the nomenclature for the variants tested may be different from the requested variants due to nomenclature differences in different isoforms of the gene. It is very important to provide us the isoform (NM number) of the gene for every variant to be tested. Result interpretation assumes that the human reference sequences are correct at the queried loci. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the collected information available at the time of reporting; additional information may exist in the future which will not be represented. Rarely, due to systematic chemical or computational issues, or human error, DNA variants may be missed. If a positive familial control specimen is not provided or available, rare errors may occur.

SIGNATURE:

Zhenbin Chen, Ph.D., CGMBS, FACMG on **Mar 9, 2024 7:44 AM**
Electronically signed

DISCLAIMER:

This test was developed and its performance characteristics determined by**Fulgent Genetics**. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at **(626) 350-0537** or **info@fulgentgenetics.com**. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

Recombine

CarrierMap™

Ordering Practice:

Practice Code: [redacted]
Fairfax Cryobank
3015 Williams Drive, #110, Fairfax, VA, 22031, US
Physician: [redacted]
Report Generated: 2017-08-07

Donor 4390

DOB: [redacted]
Gender: Male
Ethnicity: European
Procedure ID: 100056
Kit Barcode: [redacted]
Specimen: Sperm, #101432
Specimen Collection: 2015-01-12
Specimen Received: 2017-07-25
Specimen Analyzed: 2017-08-07

TEST INFORMATION

Test: CarrierMap^{SEQ} (Genotyping & Sequencing)
Panel: Custom Panel
Diseases Tested: 2
Genes Tested: 2
Genes Sequenced: 2

Partner Not Tested

SUMMARY OF RESULTS: NO MUTATIONS IDENTIFIED

Donor 4390 was not identified to carry any pathogenic mutations in the gene(s) tested.

No pathogenic mutations were identified in the genes tested, reducing but not eliminating the chance to be a carrier for the associated genetic diseases. CarrierMap assesses carrier status for genetic disease via molecular methods including targeted mutation analysis and/ or next-generation sequencing; other methodologies such as CBC and hemoglobin electrophoresis for hemoglobinopathies and enzyme analysis for Tay-Sachs disease may further refine risks for these conditions. Results should be interpreted in the context of clinical findings, family history, and/or other testing. A list of all the diseases and mutations screened for is included at the end of the report. This test does not screen for every possible genetic disease.

For additional disease information, please visit recombine.com/diseases. To speak with a Genetic Counselor, call 855.OUR.GENES.

Assay performed by Reprogenetics
CLIA ID: 31D1054821
3 Regent Street, Livingston, NJ 07039
Lab Technician: Bo Chu

Recombine CLIA # 31D2100763
Reviewed by Pere Colls, PhD, HCLD, Lab Director

Methods and Limitations

Genotyping: Genotyping is performed using the Illumina Infinium Custom HD Genotyping assay to identify mutations in the genes tested. The assay is not validated for homozygous mutations, and it is possible that individuals affected with disease may not be accurately genotyped.

Sequencing: Sequencing is performed using a custom next-generation sequencing (NGS) platform. Only the described exons for each gene listed are sequenced. Variants outside of these regions may not be identified. Some splicing mutations may not be identified. Triplet repeat expansions, intronic mutations, and large insertions and deletions may not be detected. All identified variants are curated, and determination of the likelihood of their pathogenicity is made based on examining allele frequency, segregation studies, predicted effect, functional studies, case/control studies, and other analyses. All variants identified via sequencing that are reported to cause disease in the primary scientific literature will be reported. Variants considered to be benign and variants of unknown significance (VUS) are NOT reported. In the sequencing process, interval drop-out may occur, leading to intervals of insufficient coverage. Intervals of insufficient coverage will be reported if they occur.

Limitations: In some cases, genetic variations other than that which is being assayed may interfere with mutation detection, resulting in false-negative or false-positive results. Additional sources of error include, but are not limited to: sample contamination, sample mix-up, bone marrow transplantation, blood transfusions, and technical errors. The test does not test for all forms of genetic disease, birth defects, and intellectual disability. All results should be interpreted in the context of family history; additional evaluation may be indicated based on a history of these conditions. Additional testing may be necessary to determine mutation phase in individuals identified to carry more than one mutation in the same gene. All mutations included within the genes assayed may not be detected, and additional testing may be appropriate for some individuals.

This test was developed and its performance determined by Recombine, Inc., and it has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

Diseases & Mutations Assayed

Homocystinuria Caused by CBS Deficiency (CBS): Mutations (8): ♂ Genotyping | c.919G>A (p.G307S), c.833T>C (p.I278T), c.1006C>T (p.R336C), c.959T>C (p.V320A), c.797G>A (p.R266K), c.572C>T (p.T191M), c.341C>T (p.A114V), c.969G>A (p.W324X) Sequencing | NM_001178008:3-17

Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (ACADVL): Mutations (30): ♂ Genotyping | c.779C>T (p.T260M), c.848T>C (p.V283A), c.1144A>C (p.K382Q), c.1226C>T (p.T409M), c.1322G>A (p.G441D), c.1372T>C (p.F458L), c.1405C>T (p.R469W), c.1837C>T (p.R613W), c.553G>A (p.G185S), c.739A>C (p.K247Q), c.37C>T (p.Q13X), c.265C>T (p.P89S), c.272C>A (p.P91Q), c.364A>G (p.N122D), c.388_391delGAGA (p.E130fs), c.442A>G (p.S148G), c.520G>A (p.V174M), c.856A>G (p.R286G), c.1606_1609delGCAG (p.A536fs), c.1531C>T (p.R511W), c.1512G>T (p.E504D), c.664G>A (p.G222R), c.685C>T (p.R229X), c.577G>C (p.G193R), c.881G>A (p.G294E), c.753-2A>C (IVS8-2A>C), c.1349G>A (p.R450H), c.1358G>A (p.R453Q), c.790A>G (p.K264E), c.1246G>A (p.A416T) Sequencing | NM_000018:1-20

Residual Risk Information

Detection rates are calculated from the primary literature and may not be available for all ethnic populations. The values listed below are for genotyping. Sequencing provides higher detection rates and lower residual risks for each disease. More precise values for sequencing may become available in the future.

Disease	Carrier Rate	Detection Rate	Residual Risk
Homocystinuria Caused by CBS Deficiency	♂ European: 1/224	64.29%	1/627
	♂ Irish: 1/128	70.59%	1/435
	♂ Italian: 1/224	35.71%	1/348
	♂ Norwegian: 1/41	84.38%	1/262
	♂ Qatari: 1/22	>99%	<1/2,200
	♂ Saudi Arabian: Unknown	92.31%	Unknown
Very Long-Chain Acyl-CoA Dehydrogenase Deficiency	♂ General: 1/87	66.67%	1/261

PREVENTION GENETICS

NAME	PATIENT ID
4390, Donor	2020-356-074

PATIENT INFORMATION	SPECIMEN INFORMATION	PROVIDER INFORMATION
4390, Donor ID#: FCB4390 DOB: [redacted] Sex: Male	Type: Whole Blood Collected: December 18, 2020 Received: December 21, 2020 PG ID: 2020-356-074	Harvey Stern, MD, PhD Suzanne Seitz, MS, MPA Fairfax Cryobank

MOLECULAR GENETICS REPORT:
VPS53 Gene Sequencing with CNV Detection

SUMMARY OF RESULTS: NEGATIVE

RESULTS AND INTERPRETATIONS: In this patient, for the *VPS53* gene, we found no sequence variants that are likely to be a primary cause of disease.

This patient is also apparently negative for copy number variants (CNVs) within the genomic regions of this test.

These results should be interpreted in context of clinical findings, family history and other laboratory data.

All genetic tests have limitations. See limitations and other information for this test on the following pages.

NOTE: Since this test is performed using exome capture probes, a reflex to any of our exome-based tests is available (PGxome, PGxome Custom Panels). Genetic counseling is recommended.

GENE ANALYZED: *VPS53*

SUMMARY STATISTICS:

Pipeline	Version	Average NGS Coverage	Fraction Bases Covered with NGS
Infinity_Pipeline	1.6.6	122x	100.0%

Minimum NGS coverage is ≥20x for all exons and +/-10bp of flanking DNA.

Electronically signed on December 31, 2020 by:
Renee Bend, PhD
Human Molecular Geneticist

Electronically signed and reported on December 31, 2020 by:
James L. Weber, PhD
President and Human Molecular Geneticist

SUPPLEMENTAL INFORMATION V.19.04
SEQUENCING WITH CNV DETECTION

Limitations and Other Test Notes
Interpretation of the test results is limited by the information that is currently available. Better interpretation should be possible in the future as our knowledge about human genetics and the patient's condition improve.

When Next Gen or Sanger sequencing does not reveal any difference from the reference sequence, or when a sequence variant is homozygous, we cannot be certain that we were able to detect both patient alleles. Occasionally, a patient may carry an allele which does not capture or amplify due for example to a large deletion or insertion.

Copy number variants (CNVs) of four exons or more in size are detected with sensitivity approaching 100% through analysis of Next Gen sequence data. However, sensitivity for detection of CNVs smaller than four exons is lower (we estimate ~75%).

Coverage includes all coding exons of the gene(s) analyzed plus 10 bases of flanking noncoding DNA in all available transcripts along with other non-coding regions in which pathogenic variants have been identified at PreventionGenetics or reported elsewhere.

In most cases, we are unable to determine the phase of sequence variants. In particular, when we find two likely causative variants for recessive disorders, we cannot be certain that the variants are on different chromosomes.

Our ability to detect minor sequence variants due to somatic mosaicism is limited. Sequence variants that are present in less than 50% of the patient's nucleated cells may not be detected.

Unless present within coding regions, runs of mononucleotide repeats (eg $(A)_n$ or $(T)_n$) with n >8 in the reference sequence) are generally not analyzed because of strand slippage during amplification.

Unless otherwise indicated, DNA sequence data is obtained from a specific cell type (often leukocytes from whole blood). Test reports contain no information about the DNA sequence in other cell types.

We cannot be certain that the reference sequences are correct. Genome build hg19, GRCh37 (Feb2009) is currently used as our reference in nearly all cases.

We have confidence in our ability to track a specimen once it has been received by PreventionGenetics. However, we take no responsibility for any specimen labeling errors that occur before the sample arrives at PreventionGenetics.

Genetic counseling to help to explain test results to the patients and to discuss reproductive options is recommended.

Reported results will typically not contain any additional information regarding pharmacogenetic analysis of genes, nor are these tests designed to help guide dosage requirements. Pharmacogenetic variant analysis is available, for a select list of genes, as an opt-in with PGxome® tests.

Test Methods
We use Next Generation Sequencing (NGS) technologies to cover the coding regions of the targeted genes plus 10 bases of non-coding DNA flanking each exon. As required, genomic DNA is extracted from the specimen. The DNA corresponding to these regions is captured using Agilent Clinical Research Exome hybridization

probes. Captured DNA is sequenced using Illumina's Reversible Dye Terminator (RDT) platform NovaSeq 6000 using 150 by 150 bp paired end reads (Illumina, San Diego, CA, USA).

The following quality control metrics are generally achieved: >98% of target bases are covered at >20x, and mean coverage of target bases >120x. Data analysis is performed using the internally developed software Titanium-Exome. Specified genes for which the enhance option is selected are backfilled with Sanger sequencing to achieve 100% coverage.

For Sanger sequencing, Polymerase Chain Reaction (PCR) is used to amplify the necessary exons plus additional flanking non-coding sequence. After purification of the PCR products, cycle sequencing is carried out using the ABI Big Dye Terminator v.3.1 kit. PCR products are resolved by electrophoresis on an ABI 3730xl capillary sequencer. In most cases, cycle sequencing is performed separately in both the forward and reverse directions; in some cases, sequencing is performed twice in either the forward or reverse directions.

Copy number variants (CNVs) are also detected from NGS data. We utilize a CNV calling algorithm that compares mean read depth and distribution for each target in the test sample against multiple matched controls. Neighboring target read depth and distribution and zygosity of any variants within each target region are used to reinforce CNV calls. All reported CNVs are confirmed using another technology such as aCGH, MLPA, or PCR. On occasion, it will not be technically possible to confirm a smaller CNV called by NGS. In these instances, the CNV will not be included on the report.

All differences from the reference sequences (sequence variants) are assigned to one of five interpretation categories (Pathogenic, Likely Pathogenic, Variant of Uncertain Significance, Likely Benign and Benign) per ACMG Guidelines (Richards et al. 2015). Rare and undocumented synonymous variants are nearly always classified as likely benign if there is no indication that they alter protein sequence or disrupt splicing. Benign variants are not listed in the reports, but are available upon request.

Human Genome Variation Society (HGVS) recommendations are used to describe sequence variants (http://www.hgvs.org).

FDA Notes

These results should be used in the context of available clinical findings, and should not be used as the sole basis for treatment. This test was developed and its performance characteristics determined by PreventionGenetics. US Food and Drug Administration (FDA) does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing.

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[redacted]

Patient Information:
4390, Donor
DOB: [redacted]
Sex: M
MR#: 4390
Patient#: [redacted]

Accession:
[redacted]
Test#: [redacted]
Order#: [redacted]
Ext Test#: [redacted]
Ext Order#: [redacted]
Specimen Type: DNA
Collected: Not provided
Received Date: Oct 31,2023
Authorized Date: Nov 06,2023

Physician:
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Fulgent Genetics
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Nov 14,2023**

Final Report

TEST PERFORMED

PEX6 Single Gene
(1 Gene Panel: *PEX6*; gene sequencing with deletion and duplication analysis)

RESULTS:

No clinically significant sequence or copy-number variants were identified in the submitted specimen.

A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations of the sort not queried by this test or in areas not reliably assessed by this test.

INTERPRETATION:

Notes and Recommendations:

- As requested, this report only includes variants classified as Pathogenic, Likely Pathogenic, or Risk Allele at the time of analysis. If detected, this report does not include variants classified as of uncertain significance.
- Gene specific notes and limitations may be present. See below.
- These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; https://www.nsgc.org)
- Guide to Interpreting Genomic Reports: A Genomics Toolkit (CSER Consortium; February 2017) (https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources#hep)

GENES TESTED:

PEX6 Single Gene
1 genes tested (100.00% at >20x).

PEX6

Gene Specific Notes and Limitations

No gene specific limitations apply to the genes on the tested panel.

METHODS:

4399 Santa Anita Ave.
El Monte, CA, 91731
(p) 626-350-0537 (f) 626-454-1667
info@fulgentgenetics.com
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[redacted]

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications identified by NGS are confirmed by an orthogonal method (qPCR or MLPA), unless exceeding an internally specified and validated quality score, beyond which deletions and duplications are considered real without further confirmation. New York patients: diagnostic findings are confirmed by Sanger, MLPA, or qPCR; exception SNV variants in genes for which confirmation of NGS results has been performed >=10 times may not be confirmed if identified with high quality by NGS. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

LIMITATIONS:

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to this individual's phenotype, and negative results do not rule out a genetic cause for the indication for testing. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is designed and validated for detection of germline variants only. It is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions (eg. trinucleotide or hexanucleotide repeat expansion). DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which are two or more contiguous exons in size; single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the effect of the duplication cannot be predicted. Where deletions are detected, it is not always possible to determine whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

SIGNATURE:

Dr. Harry Gao, DABMG, FACMG on **11/14/2023 08:42 AM PST**
Electronically signed

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DISCLAIMER:

This test was developed and its performance characteristics determined by**Fulgent Genetics**. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at **(626) 350-0537** or **info@fulgentgenetics.com**. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

Integrated GENETICS
LabCorp Specialty Testing Group

Tay-Sachs Enzyme Analysis

Patient Name: Donor # 4390
Referring Physician: [redacted]
Specimen #: 21632318 **Client #:** [redacted]
Patient ID: 16260354-6

DOB: Not Given
SSN: ***-**-****

Date Collected: 07/09/2014
Date Received: 07/10/2014
Lab ID:
Hospital ID:
Specimen Type: **White Blood Cells**

RESULTS: **Hexosaminidase Activity : 1814 nmol/mg protein**
Hexosaminidase Percent A: 58.9

		Plasma/Serum	WBC
Expected Non-Carrier Range:	Hex A	≥54%	≥54%
Expected Carrier Range:	Hex A	20 - 49%	20 - 49%

INTERPRETATION: NON CARRIER

This result is within the non-carrier range for Tay-Sachs disease. Less than 0.1% of patients having non-carrier levels of Hexosaminidase-A activity are Tay-Sachs carriers.

NOTE: Maximum sensitivity and specificity for Tay-Sachs disease carrier testing are achieved by using enzymology and DNA mutation analysis together.

Under the direction of: Stanford Marenberg, PHD, MDCC
Stanford Marenberg, Ph.D.

Date: 07/14/2014

Testing Performed At Esoterix Genetic Laboratories, LLC 2000 Vivigen Way Santa Fe, NM 87505 1-800-848-4436